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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,230	06/25/2004	Jac Mook Choi	YPL 0094	7458

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EXAMINER	
FRAZIER, BARBARA S	
ART UNIT	**PAPER NUMBER**
1609	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,230	CHOI ET AL.	
	Examiner	Art Unit	
	Barbara Frazier	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2004 and 26 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☒ Claim(s) *2 and 8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 June 2004 and 26 November 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Entry of amendments

1. Applicants' amendments filed 25 June 2004 and 26 November 2004 have been entered. Claims 1-11 are now pending in this application.

Priority

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

3. The listing of references in the Search Report is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609.04(a), subsection I. states, "the list ... must be submitted on a separate paper." Therefore, the references cited in the Search Report have not been considered.

Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609.05(a).

4. The information disclosure statement filed 25 June 2004 and 26 November 2004 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Drawings

5. The drawings were received on 25 June 2004 and 26 November 2004. These drawings are acceptable.

Specification

6. The disclosure is objected to because of the following informalities:

On page 4, line 20, the "ratio" is given as a range, not a ratio. It is suggested Applicants clarify by amending the specification to read "0.5-10: 1".

On page 10, line 9, "Eexample" is misspelled.

On page 11, it seems that the word "oil" is missing from Table 4, left side.

On page 13, line 12, the word "proveded" is misspelled.

Appropriate correction is required.

7. The use of the trademarks Neoral (page 1, line 18), Eudragit (page 4, line 19), and adrenol (page 5, line 3) have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks

Claim Objections

8. Claims 2 and 8 are objected to because of the following informalities: the "ratio" given in each of the claims is actually a range, not a ratio. It is suggested Applicants clarify by amending each of the claims to read "0.5-10: 1". Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 4 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 and 10 contain the trademark/trade name adrenol ™. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the

trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a chemical compound and, accordingly, the identification/description is indefinite.

11. Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 11 recites the limitation "oral pharmaceutical preparation" in line 1. There is insufficient antecedent basis for this limitation in the claim, as the phrase "oral pharmaceutical preparation" is not found in claim 1.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sherman, US 5,998,365, in view of Chen et al, US 6,267,985.

Sherman discloses a microemulsion concentrate comprising a cyclosporin dissolved in a solvent system, said solvent system comprising a hydrophilic component, a hydrophobic component, and a surfactant, wherein the hydrophobic component is propylene carbonate or polyethylene glycol having average molecular weight of less than 1000 (see claim 1, col. 9, lines 30-36). The cyclosporin of Sherman corresponds to the "active component" of the claimed invention (see claims 4, 5, 10, and 11). The hydrophobic component of Sherman may preferably be alpha-tocopherol, alpha-tocopherol acetate, and natural mixed tocopherols (see col. 4, lines 23-25). This corresponds to Applicant's use of tocopherols and tocopherol derivatives for the oil component (see page 7, lines 7 and 19-20 of the specification). Sherman also discloses that the weight ratio of the sum of oil, hydrophilic solvent, and surfactant to the active component may be 9:1 or 9.9:1 (see Examples 4-6, col. 8, lines 38 – 64). This is encompassed by Applicants'

ratio by weight of the sum of oil, hydrophilic solvent, and surfactant to the active component of 0.5-10 (claims 2 and 8). Sherman also discloses that the ratio by weight of hydrophobic component, hydrophilic component, and surfactant is 1.5:2.5:5.0, 2.0:2.0:5.0, or 1.5:3.0:5.4 (see Examples 4-6, col. 8, lines 38 – 64). This is encompassed by Applicants' ratio by weight of oil, hydrophilic solvent, and surfactant of 0.5-60:0.5-60:0.5-80 (claims 3 and 9). Sherman further discloses that the microemulsion preconcentrate composition is directly useable as drops for oral ingestion, and may be further processed by their incorporation into gelatin capsules or tablets for oral ingestion (col. 9, lines 4-11). This reads on Applicants' oral pharmaceutical preparation comprising the microemulsion preconcentrate of the claimed invention as a soft capsule, gelatin-sealed hard capsule, or liquid (claims 6 and 7). Therefore, Sherman differs from the claimed invention only in that it uses propylene carbonate or polyethylene glycol having average molecular weight of less than 1000 instead of propylene glycol diacetate or propylene glycol monoacetate as the hydrophilic solvent. However, propylene glycol monoacetate and propylene glycol diacetate are recognized solvents in the art of drug delivery systems, known for increasing the solubility of hydrophobic drugs, such as cyclosporine, and hydrophilic drugs. As evidence, Chen et al. disclose the use of propylene glycol monoacetate and propylene glycol diacetate as solubilizers for therapeutic agents (see col. 33, lines 64-67 and col. 34, lines 20-21, and claim 53, col. 54, line 40). It would have been obvious to a person skilled in the art of delivery of therapeutic agents at the time the invention was made to substitute propylene glycol monoacetate or propylene glycol diacetate for propylene carbonate or polyethylene glycol having average molecular weight of less than 1000, with a reasonable expectation of success.

With regards to Applicants' data in Experimental Example 2 on page 12 of the specification, showing improved results with the use of propylene glycol diacetate over the "conventional" microemulsion preconcentrate, which uses 1,2-propylene glycol, it is pointed out that this Example is not applicable to the above rejection, since Sherman uses propylene carbonate or polyethylene glycol having average molecular weight of less than 1000 as the solvent, not 1,2-propylene glycol.

Relevant Art

16. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Patel et al. (US 6,451,339) disclose the use of propylene glycol monoacetate and propylene glycol diacetate as solubilizers to enhance the solubility of hydrophobic therapeutic agents (see col. 25, lines 8-11 and 35-36). This reference is similar to Chen et al., above, but is limited to hydrophobic therapeutic agents.

Hong et al. (US 6,028,067) disclose cyclosporin-containing microemulsion preconcentrate composition comprising cyclosporin, lipophilic solvent, oil, and surfactant, wherein the lipophilic solvent is a carboxylic acid ester of poylyols having a high boiling point of more than 250 degrees C (see col. 5, lines 44-54). While the propylene glycol diacetate of the claimed invention falls within the range of the carboxylic acid ester polyols of Hong et al., it is noted that Applicants' claimed propylene glycol diacetate has a boiling point of 186 degrees C (page 4, line 2 of the specification), versus the 250 degrees C species of Hong et al.

Hauer et al. (US 5,342,625) disclose a microemulsion preconcentrate of cyclosporin, a hydrophilic phase which may be 1,2-propylene glycol, a lipophilic phase which is an oil, and a surfactant. It is noted that Applicants' claimed invention asserts that propylene glycol diacetate is an improvement over the use of 1,2-propylene glycol (see Experimental Example 2, page 12 of the specification).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara Frazier whose telephone number is (571)270-3496. The examiner can normally be reached on Monday-Thursday 8am-4pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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